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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of

Harukazu FUKAMI Et Al.

Serial No.: U.S. Patent Application No. 09/763,213

For: Quinazoline Derivatives and Pharmaceutical Applications Thereof

DECLARATION UNDER RULE 132

Honorable Commissioner of Patents and Trademarks
Washington D.C. 20231

Sir:

I, Tsuyoshi MUTO, a citizen of Japan, working at Suntory Biomedical Research Ltd. Japan, sincerely and solemnly declare:

That I am by profession a medicinal chemist and that I received the Ph. D. degree from Nagoya University, in March 1997, and joined Institute for Biomedical Research, Suntory Limited as a medicinal chemist in March 1997.

THAT I am an employee of the subsidiary of the assignee company of the above-identified U.S. patent application and am, therefore, completely familiar with the invention of the

above-identified U.S. patent application (i.e., "the present invention" hereinbelow) and the Office Action mailed April 25, 2002 on the above-identified U.S. patent application S.N. 09/763,213; and

THAT in order to show the patentability of the present invention over the invention set forth in the cited U.S. Patent No. 5814631 (i.e., US'631), the following Experiment was carried out under may direction and supervision.

EXPERIMENT (Comparative)

The solubilities in water of the following compounds were determined as follows.

Sample Compound

Example 13*1: 2-{3-[(7-chloro-2,4(1H,3H)-quinazolinedion-3-yl)sulfonyl]phenylaminocarbonyl}propionic acid (Compound 13)

Example 17*1: 4-[(7-chloro-2,4(1H,3H)-quinazolinedion-3-yl)sulfonyl]anthranilic acid (Compound 17)

Example 18*1: 4-[(7-chloro-2,4(1H,3H)-quinazolinedion-3-yl)sulfonyl]anthranilic acid monosodium salt (Compound 18)

Example 148*2: 3-(4-aminobenzenesulfonyl)-7-chloro-2,4(1H,3H)-quinazolinedione (Compound 148)

*1: See present application

*2: See cited US'631

Test Method

10 µl of a sample compound in DMSO solution (10 mg/mL) was mixed with 990 µl of distilled water and the mixture was subjected to an ultrasonic treatment for 5 minutes, followed by allowing to stand at room temperature. After 30 minutes, the mixture was filtered with a membrane filter (made of PVDF, a pore diameter of 0.45 µm) to remove the insoluble matters. The filtrate and a standard solution of the sample in DMSO (100 µg/mL) were analyzed by means of HPLC. The analytical results were examined, in terms of the peak areas of the both samples at 254 nm, by quantitatively determining the concentration of the sample compound and the solubility was calculated. The results are shown in Table I below.

Table I

Sample Compound	Solubility in Water (μg/mL)
Example 13	88.5
Example 17	78.9
Example 18	98.8
Example 148 of US'631	6.9

I, the undersigned declarant, declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and; further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001, of Title 18, of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Singed this day of March , 2003

Tsuyoshi MUTO